JACC Vol. 21, No. 4
March 15, 1993:866–75

Intracoronary Stenting Compared With Conventional Therapy for Abrupt Vessel Closure Complicating Coronary Angioplasty. A Matched Case-Control Study

A. MICHAEL LINCOFF, MD, ERIC J. TOPOL, MD, FACC, ANTHONY T. CHAPEKIS, MD, FACC,* BARRY S. GEORGE, MD, FACC,* RICHARD J. CANDELA, MD, FACC,* DAVID W. M. MULLER, MBBS,† CONNIE A. ZIMMERMAN, RT,* STEPHEN G. ELLIS, MD, FACC

Cleveland, Ohio; Columbus, Ohio, and Ann Arbor, Michigan

Objectives. A case-control analysis was performed to compare clinical outcome after intracoronary stenting with that after conventional therapy for abrupt vessel closure.

Background. Previous studies have demonstrated that stenting after abrupt vessel closure results in marked angiographic improvement and preservation of coronary flow, leading to the anticipation of similar improvement in clinical outcome.

Methods. Sixty-one of 92 consecutive patients treated at two clinical sites by intracoronary stenting for abrupt vessel closure were matched, according to angiographic features of closure and estimated left ventricular mass threatened by ischemia, with patients treated conventionally during the 18 months before stent availability. In 33 pairs of matched patients, vessel closure was established; in 28 pairs, it was threatened (coronary dissection or worsening stenosis with preservation of normal anterograde flow). Baseline clinical and angiographic characteristics were comparable in the two matched groups. Patients with indeterminate mechanisms of total occlusion (31%) or dissections <15 mm long (43%) predominated; patients with visible thrombus (8%) or dissections >15 mm long (18%) were infrequently represented. Stents were successfully deployed in 60 of 61 patients at a median of 52 min (range 3 to 269) after the onset of closure.

Results. When compared with conventional treatment, stenting resulted in less residual stenosis (26% vs. 49% diameter stenosis, $p < 0.001$), a greater likelihood of restoration of Thrombolysis in Myocardial Infarction (TIMI) grade 3 blood flow (97% vs. 72%, $p < 0.001$) and a reduction in the need for emergency bypass surgery (4.9% vs. 18%, $p = 0.02$). However, the incidence of Q wave myocardial infarction was nearly the same in the two groups (32% vs. 20%, respectively, p = NS). In the group with stenting, peak creatine kinase level and the frequency of Q wave infarction after established vessel closure increased with the time to stent placement ($p = 0.001$ and 0.054, respectively); the incidence of procedure-related Q wave infarction in patients who underwent stenting within 45 min of closure was very low (3.9%). In-hospital death occurred in 3.3% of patients in each treatment group. At a mean of 6.3 months of follow-up after hospital discharge, survival free from late cardiac death, myocardial infarction, bypass surgery or coronary angioplasty was 74.9% and 81.3% in the stent and the control treatment group, respectively (p = NS).

Conclusions. Although early treatment of established vessel closure by intracoronary stenting was associated with a low incidence of both myocardial infarction and emergency bypass surgery, the likelihood or severity of infarction was not reduced among those in whom stents were implanted later. Patients with threatened vessel closure could not be shown to benefit from stent treatment. These data provide preliminary indications for stent placement in the acute period to be validated in larger randomized studies.

(J Am Coll Cardiol 1993;21:866–75)

Abrupt vessel closure complicates 6% to 8% of coronary angioplasty procedures, resulting in death, myocardial infarction or emergency bypass surgery in more than 50% of these patients (1,2). Moreover, patients with angiographic evidence of coronary dissection or thrombus without immediate vessel closure may develop delayed ischemic complications after leaving the catheterization laboratory (3–5); these patients with "threatened" closure also represent a management challenge.

Originally envisioned by Dotter (6) as a therapy for restenosis following coronary angioplasty, intracoronary stent placement is also under investigation as a treatment for established or threatened abrupt vessel closure. By virtue of its ability to scaffold the arterial wall and improve the caliber of the true lumen after dissection, limit elastic recoil or spasm and optimize blood flow, stents have been shown to produce highly satisfactory immediate angiographic results after coronary disruption or occlusion (7–9). Encouraging

From the Department of Cardiology, The Cleveland Clinic Foundation, Cleveland, Ohio, *Mid-Ohio Cardiology Research Foundation, Riverside Methodist Hospital, Columbus, Ohio and †Division of Cardiology, Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, Michigan.

Manuscript received June 17, 1992; revised manuscript received August 21, 1992, accepted September 1, 1992.

Address for correspondence: Stephen G. Ellis, MD, Sones Cardiac Catheterization Laboratory, The Cleveland Clinic Foundation, F25, 9500 Euclid Avenue, Cleveland, Ohio 44195.

0735-1097/93/$6.00

Table 1. Definition of Angiographic Variables

Established abrupt vessel closure
Worsening stenosis with Thrombolysis in Myocardial Infarction (TIMI) (13) grade 0–2 distal flow in a previously patent vessel (TIMI 3), during or after coronary angioplasty, within the period of hospitalization. Abrupt closure of a previously totally occluded vessel was defined as closure after establishment of TIMI grade 3 flow by initially successful dilation.

Threatened abrupt vessel closure
Angiographic appearance during or after coronary angioplasty thought likely to be at increased risk for subsequent development of abrupt closure (e.g., dissection or intraluminal thrombus), despite preservation of normal TIMI grade 3 flow beyond the lesion.

Jeopardy score
Estimate of the mass of myocardium at potential risk for ischemia or infarction in the event of abrupt vessel closure (14,15).

Coronary dissection
Presence of a curvilinear filling defect parallel to the vessel lumen, contrast medium outside of the vessel lumen persisting after passage of contrast medium or a spiral defect obstructing the vessel lumen.

Coronary thrombus
Presence of discrete or mobile intraluminal filling defects at the site of closure.

Indeterminate closure morphology
Vessel angiographic appearance of a radiolucent lumen irregularity or persistent filling defect that is neither discrete nor mobile.

Restenosis
≥50% diameter stenosis at the previous angioplasty/abrupt closure site on subsequent cardiac catheterization.

short-term angiographic results in patients with abrupt vessel closure obtained with several stents, including the Gianturco-Roubin stent (7,10), have led to the expectation of similar improvements in clinical outcome. However, these devices may be associated with such adverse effects as stent thrombosis, bleeding complications due to anticoagulation, and late restenosis (9,11,12), and difficulties or delay in stent placement may lead to substantial myocardial necrosis despite eventual restoration of an adequate vessel lumen. It is therefore uncertain whether stenting offers an advantage with respect to major clinical end points such as death, coronary bypass surgery or myocardial infarction over conventional therapy for abrupt closure. We thus performed a case-control analysis to compare clinical outcome after intracoronary stenting with that in matched patients treated conventionally for established or threatened abrupt vessel closure.

Methods

Patients with stenting. The Gianturco-Roubin intracoronary stent, a balloon-expandable flexible stainless steel coil, has been available for clinical investigation since December 18, 1989 at the Riverside Methodist Hospital and February 1, 1990 at the University of Michigan Medical Center. All patients in whom stent placement was attempted through June 30, 1991 for threatened or established abrupt vessel closure (see Table 1 for definitions) at the two institutions were considered for the study. Those patients in whom abrupt closure occurred in the setting of angioplasty for acute myocardial infarction (n = 1), after previously treated abrupt closure of the same lesion (n = 2), after use of another investigational device (intracoronary laser [n = 1]), or for whom adequate angiographic views of closure were not recorded on film (n = 3) were excluded. A total of 92 of 99 patients met these criteria and form the basis of this study.

Control group. For case-control matching with the group with stenting, conventionally treated patients with threatened or established abrupt vessel closure were identified by retrospective review of the clinical angioplasty data bases at the two institutions. These patients, who would have been potential candidates for stenting had these devices been available, were treated during the period from July 1, 1988 until the availability of stents and during the interval between January 20, 1991 and March 20, 1991 when stents were not used because of a temporary protocol hold by the Circulatory Systems Device Bureau of the Food and Drug Administration. Patients in whom closure was not managed with stents despite the availability of stents were not included in the control population, as bias in the selection of their therapy could not be retrospectively excluded. Criteria for selection of patients to review as possible control subjects included documentation in the catheterization laboratory record of established vessel closure, intracoronary thrombus or dissection, emergency coronary bypass surgery, prolonged balloon inflations (>120 s), thrombolytic therapy or use of an autoperfusion (Stack) balloon catheter. Patients treated for acute myocardial infarction or with investigational devices were excluded. Also excluded were patients in whom the guide wire could not be passed across the zone of occlusion, as these patients did not represent a group in whom intracoronary stenting could have been performed. Cineangiographic films were unavailable for review or did not show adequate views of the abrupt closure in 17 patients. A total of 78 patients met these criteria for the control group and were thus potential candidates for matching.

Treatment of abrupt vessel closure. Coronary angioplasty was performed by methods described in detail elsewhere (16). Abrupt or threatened vessel closure was managed at the individual operator's discretion without a uniform protocol; "conventional therapy" performed in the catheterization laboratory included administration of nitrates, additional heparin or thrombolytic agents and the use of prolonged balloon inflations (with or without an autoperfusion catheter), intraaortic balloon counterpulsation or percutaneous femoral cardiopulmonary bypass. Since its availability for investigation at the two clinical sites, the Gianturco-Roubin stent has been employed by protocol during various stages of the management of established or threatened abrupt vessel closure (10). In some patients, stenting was performed immediately after closure without attempts at conventional therapy if the operator judged that conventional therapy would be unsuccessful in treating a lesion such as extensive

Table 2. Comparison of Baseline Clinical and Angiographic Variables for Matched Patients

	Patients With Stenting	Control Patients
Clinical variables		
Age (mean, yr)	57.6	60.1
Male gender (%)	71	61
Diabetes mellitus (%)	26	25
Unstable angina (postinfarction, rest or accelerated exertional angina) (%)	89*	59*
Post MI (%)	30	30
Previous MI (%)	46	53
Angiographic variables		
Jeopardy score (1–6)	2.43	2.51
ACC/AHA score B_2 or C (%)	33	34
LV ejection fraction (%)	55	53
Diseased vessels (no.)	1.6	1.8
Target % stenosis	69	72

*p = 0.001. No other differences were significant (p < 0.10). ACC/AHA score = modified American College of Cardiology/American Heart Association Task Force stenosis score (17,18); LV = left ventricle; MI = myocardial infarction.

coronary dissection. In other patients, stents were used only after closure proved to be refractory to brief or prolonged attempts at therapy with a variety of modalities, including autoperfusion angioplasty and thrombolytic agents. After stenting, patients were treated with a dextran infusion for 10 to 24 h, continuous intravenous heparin to maintain a partial thromboplastin time of 2 to 2.5 times the control value until the prothrombin time was within the therapeutic range, sodium warfarin (Coumadin) to achieve a prothrombin time of 1.5 to 1.7 times the control value for 3 months, and long-term oral aspirin and dipyridamole.

Clinical and procedural variables and follow-up after hospital discharge. Baseline and procedural variables, hospital outcome after angioplasty and data on complications were obtained from catheterization laboratory and hospital medical records. Clinical variables assessed are enumerated in Tables 2 to 4.

Patients were followed up after hospital discharge for the occurrence of late cardiac events or ischemic symptoms. Per protocol, all patients receiving stents were requested to undergo thallium exercise or pharmacologic stress testing and cardiac catheterization at 4 and 6 months, respectively. Stress testing was performed in conventionally treated con-

Table 3. Comparison of Closure and Procedural Variables for Matched Patients

	Established AVC (33 pairs)		Threatened AVC (28 pairs)	
	Patients With Stenting	Control Patients	Patients With Stenting	Control Patients
Closure variables				
Closure vessel (%)				
Left anterior descending	49	33	46	36
Left circumflex	27	24	18	18
Right coronary	18	40	29	46
Left main	3	3	7	0
Saphenous vein graft	3	0	0	0
% stenosis	93	90	54	50
TIMI flow grade 0 or 1 (%)	61	70	0	0
Median dissection (mm)	9.0	15	7.0	8.0
(interquartile range)	(5.0–21)	(7.5–37)	(4.0–12)	(4.0–12)
Filling defect (%)	3.2	6.1	7.1	7.1
ECG changes (%)	83	90	60	54
Systolic BP <90 mm Hg (%)	30	15	8	9
Out-of-laboratory closure (%)	28	22	19	11
Procedural variables				
Repeat balloon angioplasty (%)	97	88	100	96
Median inflation (min)	5.0	4.0	5.0*	7.0*
(interquartile range)	(2.9–10)	(3.0–9.5)	(2.9–8.0)	(4.0–10)
Autoperfusion angioplasty (%)	24†	6†	29	29
Thrombolytic agents (%)	33	42	14	32
IABP (%)	12	15	7.1	0
CPS (%)	3	0	3.6	3.6

*p = 0.04 comparing patients with stenting and control patients in the group with threatened vessel closure. †p = 0.07 comparing patients with autoperfusion angioplasty in the group with established vessel closure. No other differences were significant (p < 0.10). AVC = abrupt vessel closure; BP = arterial blood pressure; CPS = percutaneous cardiopulmonary support; ECG changes = ischemic electrocardiographic changes (ST segment elevation or depression or T wave inversion or peaking); IABP = intraaortic balloon pump; TIMI = Thrombolysis in Myocardial Infarction.

Table 4. Comparison of In-Hospital Outcome for Matched Patients With Stenting and Control Patients

	Total Group (61 pairs)			Established AVC (33 pairs)			Threatened AVC (28 pairs)		
	Patients With Stenting	Control Patients	p Value	Patients With Stenting	Control Patients	p Value	Patients With Stenting	Control Patients	p Value
Procedural outcome									
Residual % diameter stenosis	26	49	< 0.001	22	53	< 0.001	31	43	0.028
TIMI grade 3 flow restored (%)	97	72	< 0.001	97	58	< 0.001	96	89	NS
ECG changes resolved (%)	55	39	NS	60	38	NS	47	42	NS
Clinical outcome									
Death (%)	3.3	3.3	NS	6.1	6.1	NS	0	0	NS
Q wave MI (%)	32	20	NS	44	25	NS	18	16	NS
Emergency CABG (%)	4.9	18	0.021	9.1	27	0.070	0	7.1	NS
Non-Q wave MI (%)	11	31	0.039	16	40	NS	4	21	NS
Peak serum CK (mean, IU/liter)*	2,400	1,300	0.018	2,700	1,300	0.016	1,400	1,300	NS
Late vessel reclosure (%)	13	12	NS	15	6.3	NS	11	18	NS
Hospital stay (days)†	11	7.8	0.019	10	8.1	NS	12	7.4	0.044
Blood transfusion‡									
Median (units)	3	5	NS	2	6	0.058	4	2	0.047
Range (units)	(1–59)	(1–18)		(1–59)	(2–18)		(2–37)	(1–6)	

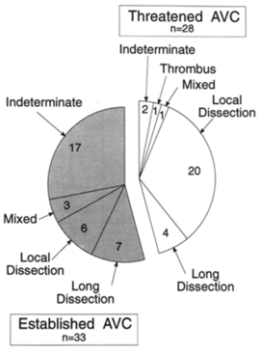
*Mean peak serum creatine kinase (CK) among patients with a myocardial infarction. †Postprocedure. ‡Median transfusion requirement among patients requiring transfusions. CABG = coronary artery bypass grafting surgery; other abbreviations and definitions as in Tables 2 and 3.

trol subjects if they developed recurrent symptoms or if it was requested by their attending physician; cardiac catheterization was reserved for those in whom results of a stress study were abnormal. Follow-up clinical data were obtained by an observer who had no knowledge of in-hospital outcome by review of medical records and cineangiograms and by telephone contact with the patient or the attending physician, or both. End points after hospital discharge consisted of late death, myocardial infarction, coronary bypass surgery, coronary angioplasty, recurrent angina and results of exercise testing and cardiac catheterization.

Angiographic analysis and case-control assignment. Cineangiographic films were independently analyzed by two experienced angiographers who had no knowledge of clinical outcome; discrepancies in interpretations of closure morphology, coronary flow or diameter stenoses were resolved by consensus. Evaluation of closure-related coronary morphology and jeopardy score (14) was performed without knowledge of subsequent therapy, although analyses after vessel closure could not be conducted in blinded manner because of the recognizable angiographic configuration of the Gianturco-Roubin stent. Hand-held calipers were used to measure percent diameter stenoses and lesion length at end-diastole in a non-foreshortened projection demonstrating the most severe coronary stenosis. Selected angiographic terms are defined in Table 1.

Abrupt vessel closure was classified according to one of 10 prospectively defined closure types (Fig. 1): established versus threatened closure due to thrombus, dissection length <15 mm, dissection length ≥15 mm, both thrombus and dissection, or indeterminate mechanisms. Patients with and without stenting were matched by random allocation within cells defined by closure type and jeopardy score; exact matches were required by closure type, and matches within 1 jeopardy score point were accepted. A total of 61 stent-control pairs were assigned in this manner; 31 stent-treated patients remained unmatched because of the limited number of suitable control patients.

Figure 1. Angiographic morphology of closure in 61 matched pairs of patients with stenting and control patients. Shaded sections represent the 33 matched pairs with established abrupt vessel closure (AVC); white sections represent 28 patient pairs with threatened vessel closure; the numbers within the sections denote patient pairs. Local dissection = dissection length <15 mm; long dissection = dissection length ≥ 15 mm; mixed = presence of both dissection and thrombus.



Statistical analysis. Continuous variables were expressed as mean value ± 1 SD, with differences assessed by the Student paired or unpaired *t* test. Variables with a nongaussian distribution were described with median and range or interquartile values. Paired and unpaired binomial variables were compared using the sign and Fisher chi-square significance tests, respectively. Differences between paired and unpaired ordinal categoric variables were assessed for significance by the Wilcoxon and Mann-Whitney tests, respectively. All p values ≤ 0.10 were reported; $p > 0.10$ was designated as nonsignificant (NS). Multivariate logistic analysis was used to detect association between baseline or procedural variables and clinical outcome. Event-free survival analysis was performed by the Kaplan-Meier method, with significance testing by the Mantel log-rank test; events analyzed consisted of late death, myocardial infarction, coronary bypass surgery or repeat coronary angioplasty. Analyses were performed with the System for Statistics (SYSTAT).

Myocardial infarction was chosen to be the primary end point for determination of adequate sample size. With an expected 50% incidence of post-procedural infarction among control patients, the sample size required to detect a 50% reduction in this incidence with an 80% power and a 95% significance level was 65 patients in each treatment group.

Results

Baseline characteristics. Of the 92 patients who received a stent for abrupt vessel closure during the study period, 61 were matched for this analysis with control subjects who did not undergo stenting. Of these, 33 (54%) were treated for established vessel closure and 28 (46%) for threatened closure.

Table 2 demonstrates that matched patients with and without stenting were comparable with respect to most baseline clinical and angiographic characteristics. Although a significant difference in the incidence of unstable angina was noted between groups, this variable did not prove to be an independent correlate of final procedural outcome by logistic analysis.

Unmatched patients with stenting. To determine whether the 61 matched patients with stenting were a representative sample of the total group of 92 patients who received a stent, baseline characteristics were compared between the matched and unmatched groups of patients with stenting. There were no significant differences between matched and unmatched patients in any of the 11 variables listed in Table 2.

Profile and management of abrupt vessel closure. The distribution of the 61 matched patient pairs according to 10 classifications of closure type is summarized in Figure 1. Notably, intraluminal thrombus was identified in relatively few patients (8%) in this study.

Table 3 compares matched patients with and without stenting with respect to the characteristics and in-laboratory management of abrupt vessel closure. Importantly, matched pairs proved to be similar; the two groups differed only by the slightly longer median balloon inflation times in patients with threatened closure without stenting. Nearly all patients were treated with repeat balloon angioplasty; inflation times ranged from 1 to 31 min (median for the entire group 5 min). Dilation with a Stack autoperfusion balloon was performed in 26 (21%) of 122 patients for a median duration of 10 min.

Stent deployment. Intracoronary stents were successfully deployed in 60 (98%) of the 61 matched patients in whom deployment was attempted at a median of 52 min from the onset of vessel closure (range 3 to 269 min). Time to stent placement was significantly shorter among patients whose vessel closed in the catheterization laboratory (median 40 min, range 3 to 207) than in the 23 patients whose vessel closed while they were on the inpatient ward (median 130 min, range 77 to 269 min, $p < 0.001$). A single stent was implanted in 56 patients, two stents each were implanted in 4 patients, and 1 patient received three stents to treat a 72-mm dissection of the right coronary artery. Thus, a total of 67 stents were implanted in 61 patients; of these, 2, 21, 32, 10 and 2 were 2, 2.5, 3, 3.5 and 4 mm in diameter, respectively.

In only 20 (33%) of 61 patients was stenting performed without preceding attempts at management by prolonged balloon inflations (≥5 min) or administration of thrombolytic agents. Among the 41 patients who underwent therapy for closure before stent implantation, 26 were treated with prolonged balloon inflations only, 6 with thrombolytic agents only and 9 with both.

Unmatched patients with stenting. Comparison of closure and management variables between matched and unmatched patients with stenting demonstrated that the two groups differed most significantly in the proportion of patients with extensive dissections (18% of matched vs. 68% of unmatched patients, $p < 0.001$) because of the limited number of control patients with long dissections. Additionally, there were differences in the mean percent stenosis (93 ± 15% for matched vs. 79 ± 16% for unmatched, $p = 0.005$) and mean distal Thrombolysis in Myocardial Infarction (TIMI) (3) grade flow (70% TIMI flow ≤1 for matched vs. 22% TIMI flow ≤1 for unmatched, $p < 0.001$) after established abrupt vessel closure.

In-hospital procedural and clinical outcome. In-hospital outcome for matched patients with and without stenting is summarized in Table 4.

Procedural outcome. Compared with conventional therapy, intracoronary stenting for abrupt vessel closure produced a significantly superior immediate angiographic result as manifested by residual lesion diameter stenosis and restoration of TIMI grade 3 flow across the zone of occlusion; this beneficial effect was most apparent in patients with established rather than threatened closure. Normal coronary flow was successfully reestablished in all but 2 of 61 patients in whom stents were employed. Patients treated with stents

required emergency bypass surgery less frequently than did control patients (4.9% vs. 18%, p = 0.021).

Myocardial infarction and death. Other clinical end points did not consistently reflect the procedural benefit initially imparted by stenting. Two patients with established vessel closure in each treatment group died: two of cardiogenic shock resulting from abrupt closure, one after in-hospital reclosure and one of multiple organ failure 13 days after stent placement. Similarly, there were no significant differences between patients managed with stents and those who received conventional therapy in the combined rates of infarction (Q wave and non-Q wave) (43% and 51%, respectively, among patients with and without stenting, p = NS). Peak serum creatine kinase (CK) levels among patients with a myocardial infarction were significantly higher in those treated with stents for established closure (mean peak CK = 2,700 vs. 1,300 IU/liter for patients with and without stenting, p = 0.016); there was no difference in the peak CK values of patients who had an infarction after threatened closure (mean peak CK 1,400 vs. 1,300 IU/liter for patients with and without stenting, p = NS).

Correlates of infarction in the group with stenting. Periprocedural Q wave myocardial infarction rates (excluding infarction due to late reclosure) and peak CK levels among the entire group of matched and unmatched patients treated with stents for established vessel closure were directly related to the time to stent placement after the onset of closure (p = 0.054 for Q wave myocardial infarction; p = 0.001 for peak CK) (Fig. 2). In patients with threatened closure, a similar, though nonsignificant association between peak CK and time to stent implantation was observed, whereas peak CK was also related inversely to final TIMI flow grade (p < 0.001). By multivariate analysis, both the occurrence of vessel closure outside of the laboratory and the use of prolonged (≥5 min) balloon inflations or thrombolytic therapy before stenting were independently associated with a markedly increased risk for periprocedural Q wave myocardial infarction (risk ratio 4.8, p = 0.034 for out-of-laboratory closure; risk ratio 5.2, p = 0.037 for use of prolonged balloon inflations or thrombolytic therapy).

Late reclosure. In-hospital reclosure of the previously treated closure site occurred in 13% and 12%, respectively, of patients with and without stenting. There was no relation between stent size and the incidence of in-hospital reclosure. The occurrence of vessel reclosure was significantly associated with an increased risk for Q wave myocardial infarction (odds ratio 9.5, p < 0.001), a higher peak serum CK level (mean 1,700 vs. 800 IU/liter with and without reclosure, respectively, p < 0.001), and a longer postprocedural hospitalization course (mean 14.7 ± 7.4 days vs. 8.8 ± 7.2 days with and without reclosure, respectively, p = 0.012). Nonsignificant trends toward excess risk for death and emergency coronary bypass surgery in patients with reclosure were also noted.

Duration of hospital stay and blood transfusions. The mean duration of the hospital stay after abrupt vessel closure was 3.2 days longer in patients with than in those without stenting (p = 0.019); prolongation of the hospital period was greatest in patients with threatened vessel closure (Table 4). Blood transfusions were administered with equal frequency in the two groups (49% vs. 41%, respectively, p = NS), although significantly more transfusion units were required among patients with stenting than among control patients with threatened closure (median 4 units vs. 2 units, respectively, p = 0.047). In patients with stenting, blood transfusions were most commonly required as a result of femoral artery or retroperitoneal hemorrhage (57%), although 13% and 17%, respectively, of patients received transfusions because of coronary bypass surgery or gastrointestinal bleeding. Coronary bypass surgery was the most frequent cause of transfusions among control patients (48%), with major femoral puncture site hemorrhage requiring transfusions in 40%.

Subset analysis. Clinical outcome was separately analyzed in the four predominant morphologic subsets comprising 50 of the 61 pairs of matched patients (Table 5): established vessel closure due to indeterminate mechanism, localized dissection, or long (≥15 mm) dissection and threatened closure due to localized dissection. Outcome was not significantly different for patients with and without stenting in any of these groups. Moreover, comparison of the 61 matched patients with stenting with the unmatched group of 31 patients with stenting revealed no significant differences in rates of death, infarction or emergency bypass surgery.

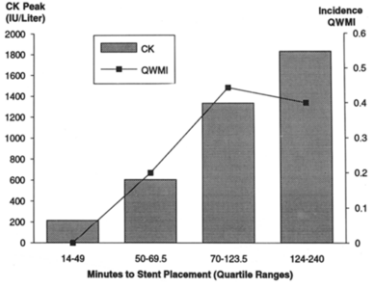


Figure 2. Association between the incidence of periprocedural Q wave myocardial infarction (QWMI) and peak serum creatine kinase level (CK), and the interval from abrupt vessel closure to stent deployment in 41 matched and unmatched patients with stenting after established closure. Patients with in-hospital reclosure of the stented vessel (seven patients) or in whom the time to stenting was not available (three patients) are excluded. Time intervals are expressed as quartile ranges; the median time to stenting was 69.5 min. There is a significant correlation between CK peak and time to stent placement (p = 0.001) and a less significant association (p = 0.054) between the incidence of Q wave infarction and time to stenting.

Table 5. Clinical Outcome by Major Morphologic Subgroups

Closure Morphology	n	Emergency CABG (%) Patients With Stenting	Emergency CABG (%) Control Patients	Q Wave MI (%) Patients With Stenting	Q Wave MI (%) Control Patients	Non-Q Wave MI (%) Patients With Stenting	Non-Q Wave MI (%) Control Patients
Established closure							
Indeterminate	17	6	24	53	33	6*	55*
Local dissection†	6	0	17	17	20	40	0
Long dissection‡	7	14	43	33	0	33	50
Threatened closure							
Local dissection	20	0	10	15	15	0	14

*$p = 0.063$, $p > 0.10$ for all other differences between patients with stenting and control patients. †Dissection length <15 mm. ‡Dissection length ≥15 mm. Abbreviations as in Tables 2 and 4.

Intermediate-term outcome. Of the 118 patients in the matched study group surviving to hospital discharge, data after hospital discharge were obtained for 116 (98.3%). The mean duration of follow-up was 6.3 months (range 0.5 to 17) for patients with stenting and 15 months (range 2 to 36) for control patients; the full duration of follow-up for the two groups differed because stents were implanted during the period after December 1989, whereas the majority of vessel closures in the control patients occurred before that time. However, all observed cardiac events (late death, myocardial infarction, bypass surgery or coronary angioplasty) occurred within the 1st 7 months after hospital discharge.

Actuarial survival at 7 months for the 116 matched patients was 96.5%. Of the 59 patients who received intracoronary stents, 1 died suddenly, 1 had a late myocardial infarction and 6 each underwent bypass surgery and coronary angioplasty during the follow-up period. Among 57 conventionally treated control patients, there were three cardiac deaths, no late myocardial infarctions, three bypass operations and four angioplasty procedures. Actuarial event-free survival after hospital discharge at 7 months (Fig. 3) was 74.9% and 81.3%, respectively, for patients with and without stenting (p = NS). Subset analysis by established or threatened vessel closure also failed to demonstrate a significant difference in late outcome between the treatment groups.

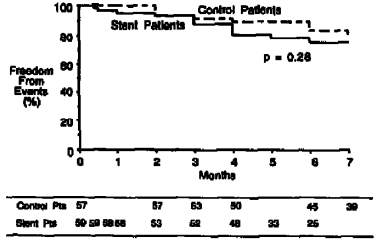
Extension of survival analysis to include both in-hospital and postdischarge cardiac events was performed to determine if stent implantation was associated with any event-free survival benefit when measured from the time of occurrence of abrupt closure. By 7 months after hospital discharge, 41.4% and 46.1%, respectively, of patients treated with stenting and conventional therapy remained free of cardiac events (p = NS). No significant differences in outcome between patients with and without stenting was noted for the subsets with established or threatened vessel closure.

By the latest date of clinical follow-up, anginal symptoms were present in 15 (26%) of 58 patients with and 21 (39%) of 54 patients without stenting. Follow-up exercise or pharmacologic stress testing at ≥4 months after abrupt vessel closure was performed in 74% of 49 eligible patients with stenting; of 50 eligible control patients, stress testing was performed in 39%. Myocardial ischemia in any coronary distribution was detected in 39% and 32%, respectively, of patients with and without stenting in whom stress testing was performed. Cardiac catheterization in 33 of 42 patients with stenting (6 months after stenting in asymptomatic patients or earlier in those with recurrent ischemia or cardiac events) demonstrated restenosis at the site of previous closure in 15 (46%). Of control patients, catheterization was performed after initial hospital discharge on clinical grounds in 13, of whom 9 (69%) had developed restenosis.

Discussion

Abrupt vessel closure complicates 6% to 8% of coronary angioplasty procedures (1,2,4,19,20). A variety of management strategies, including prolonged or perfusion balloon angioplasty (21–23), laser balloon angioplasty (24,25), coronary atherectomy (26) and administration of thrombolytic

Figure 3. Kaplan-Meier curve of freedom from late cardiac events (death, myocardial infarction, coronary bypass surgery or coronary angioplasty) in 59 patients (Pts) with stenting (Stent) and 57 control patients surviving to hospital discharge. There is no significant difference between the two groups in event-free survival after hospital discharge.



agents (1,27), have been used to reverse abrupt closure in the cardiac catheterization laboratory. Nevertheless, conventionally treated periprocedural vessel closure still carries a 2% to 8% risk of death, a 20% to 40% risk of myocardial infarction and a 20% to 55% risk of emergency bypass surgery (1,2,4,19,20); no investigational therapy has yet been found to be superior to coronary angioplasty in this regard.

Early reports have suggested that intracoronary placement of the Gianturco-Roubin (7,10), Medinvent (8,11) or Palmaz-Schatz (9) stent may be an effective technique for restoring and stabilizing vessel patency after abrupt vessel closure, thereby reducing the need for emergency bypass surgery. The concomitant risks are not insignificant, however, and have included thrombotic stent occlusion despite anticoagulation (9–11) and fatal intracranial hemorrhage (11). No prior study has compared clinical outcome in patients treated with stents with that in a similar group of patients managed conventionally for abrupt closure, nor have the role and timing of stenting for threatened and established closure been independently examined.

Design of the current study. For established or threatened abrupt vessel closure, stenting may be used as a primary strategy or as a fallback technique for closures that prove refractory to conventional therapy. To provide a preliminary paradigm of a management strategy in these settings, the current study extends previous reports by focusing on the impact of stenting on the in-hospital and intermediate-term clinical sequelae of abrupt closure. A matched case-control analysis was performed to compare outcome after intracoronary stenting with that achieved by conventional therapy. The study group was uniform in that only one stent device was employed, the Gianturco-Roubin coil, but the results of this analysis may consequently be extrapolated only with caution to other types of stents. The number of baseline characteristics to which patients with stenting could be matched was limited by the size of the control patient pool. Therefore, case-control matching was prospectively performed utilizing those variables that, based on prior observations (3–5,14,15,20,28,29), were most likely to affect overall outcome and the efficacy of stenting relative to conventional therapy.

Effectiveness of stenting for established abrupt closure. Intracoronary stenting successfully restored normal TIMI grade 3 flow in 97% of patients with established vessel closure, more than two-thirds of whom had failed to benefit from preceding attempts at conventional therapy. As a result, there was a threefold reduction in the number of patients with stenting who required emergency bypass surgery relative to the conventionally treated control patients. These data, consistent with earlier reports (7,8), highlight the extraordinary effectiveness of the intracoronary stent in reestablishing stable angiographic patency after coronary disruption.

By this analysis, however, other measurements of clinical outcome were the same among patients with and without stenting. Despite the immediate benefit of improved angiographic patency and the reduced need for emergency bypass surgery, the frequency of Q wave myocardial infarction in the group with stenting was substantial (44%) and not significantly different from that in the control group. This finding was somewhat unexpected; in view of the reported 20% to 60% rate of Q wave myocardial infarction among patients who require emergency bypass surgery for abrupt vessel closure (30,31), the diminished need for emergency surgery in patients managed with stents would have been anticipated to translate into a lower risk for subsequent Q wave infarction.

Importance of time to stent placement. Both the incidence of Q wave infarction and peak CK levels were associated with the time to stent placement (Fig. 2). The period from recognition of vessel closure until stent implantation was a median of >1 h and exceeded 2 h in 13 patients (27%). Among patients in whom the stent was deployed within 49 min (first quartile), there were no periprocedural (unrelated to late reclosure) Q wave infarctions and the mean peak CK level was only 213 IU/liter; both infarction rate and CK level increased markedly with time to stent placement.

In some patients, delay in stenting was the unavoidable consequence of the time required to return a patient to the catheterization suite, manage hemodynamic instability or recross the zone of occlusion with a guide wire and deploy the stent. However, in many patients, the interval between vessel closure and stenting also reflected the time during which other treatment strategies were attempted before the decision to place a stent was made. In fact, compared with immediate treatment with a stent, administration of thrombolytic agents or prolonged (≥5 min) balloon inflations before stenting were independently associated with a greater likelihood of sustaining a Q wave infarction. Thus, during this early experience at two institutions with stenting for abrupt closure, use of the stent as a final "bailout" technique in >66% of patients was associated with the high observed rate of Q wave myocardial infarction. In view of the extraordinary effectiveness of the stent in reestablishing coronary patency, however, clinical outcome after stenting for abrupt vessel closure may be improved by prompt triage of patients to stent placement without a prolonged antecedent period of conventional therapy.

Other factors. The similarity in infarction rates among patients with and without stenting did not appear to be due to the occurrence of late in-hospital vessel reclosure. The frequency of reclosure was not significantly different in the two groups, and analysis of data excluding those patients with reclosure still demonstrated that the incidences of Q wave infarction was the same in patients with and without stenting.

Effectiveness of stenting for threatened vessel closure. There were no significant differences in the incidence of death or myocardial infarction or in peak CK levels between patients with and without stenting in the group with threatened closure, despite a slightly greater efficacy of stenting in the reduction of residual lesion stenosis in this group (Table

4). None of the 28 patients with stenting required emergency bypass surgery, compared with 2 of 28 control patients (7.1%) (p = NS). Patients with threatened closure appeared better able to tolerate delay in stent placement than did those with established closure; Q wave myocardial infarction rates were lower and the association between time to stenting and peak CK level was less significant in the threatened closure group. Importantly, patients treated with stents for threatened closure had greater transfusion requirements and required a longer postprocedure hospitalization time than did conventionally treated control subjects (Table 4). Thus, stenting could not be demonstrated to improve outcome in the group of patients with threatened, rather than established, abrupt closure, but had an adverse effect on transfusion requirements and length of hospital stay.

In-hospital reclosure and late clinical events. Among patients treated for established or threatened vessel closure, in-hospital reclosure of thrombotic or indeterminate angiographic morphology occurred in 13% and 12% of the stented and control groups, respectively. Although the number of patients experiencing late reclosure was small, this finding suggests that the improved angiographic appearance and blood flow at the closure site produced by the stent may not entirely compensate for the device's thrombogenicity. As in the setting of acute myocardial infarction (32), late reocclusion after treated abrupt closure in the present series was associated with substantial morbidity.

Late clinical outcome after hospital discharge, as measured by freedom from cardiac death, myocardial infarction, coronary bypass surgery or coronary angioplasty, was similar in the patients with and without stenting. Although clinical events occurred too infrequently for survival analysis to be applied to detect significant differences in individual end points, patients with stenting tended to undergo revascularization procedures more frequently than did control subjects after hospital discharge (20% vs. 12%, respectively). This trend likely reflects the substantially greater number of control patients than of patients with stenting (18% vs. 4.9%) who required emergency bypass surgery during the hospital stay. The 46% incidence of restenosis among patients with stenting in the present cohort is comparable to the 33% to 57% restenosis rates reported in other series of patients with stent-treated (9,10,33) or conventionally managed (34,35) abrupt closure.

Clinical outcome in morphologic subsets. The clinical efficacy of stenting relative to conventional therapy was the same in each of the four predominant morphologic subgroups studied (Table 6). However, because of the small sample sizes in these individual subgroups, the statistical power to detect clinically relevant improvements in outcome by stenting was low. It is therefore possible that treatment with stents may be most beneficial in certain groups of patients defined by their angiographic morphology of closure; in particular, these overall results should be applied with caution to patients with extensive coronary dissections who were infrequently represented in this analysis.

Limitations. The current study has several important limitations. 1) This was a nonrandomized, retrospective analysis using a historical control population; the two treatment periods were consecutive, however, without substantial changes in management strategy aside from the availability of stents. 2) Although the time to stent placement was associated with a lower incidence and extent of periprocedural infarction in this series, the analogous time to reperfusion among conventionally managed control patients was not available. Thus, although this analysis suggests that rapid stent deployment favorably influences clinical outcome after abrupt closure, it cannot establish whether prompt restoration of patency by stenting is superior to rapid recanalization by conventional techniques with regard to clinical end points. Moreover, as the effects of all potential confounding patient characteristics cannot be retrospectively controlled, an independent correlation between time to stent placement and clinical outcome is not definitive. 3) This study describes the earliest experience with stenting at two institutions, and it is possible that increased familiarity and the learning curve of operator experience with the new device might result in improved clinical results. 4) Among patients in whom myocardial reperfusion occurs, the magnitude of the peak CK level may overestimate the extent of myocardial infarction (36); the use of this variable as a clinical end point in this study may thus have biased against stent therapy with its higher rate of restoration of angiographic patency. Postprocedure left ventriculography and regional wall motion analysis, better measures of the extent of infarction, were not assessed in the majority of patients in this series. 5) One third of the patients with stenting could not be paired with appropriately matched control patients, and a disproportionate number of these unmatched patients had had an extensive dissection at the closure site. However, comparison of baseline, intraprocedural and outcome characteristics demonstrated few significant differences between the matched and nonmatched groups, even in the subset of patients with long dissections; it is likely, therefore, that patients included in the paired analysis were otherwise representative of the entire cohort. 6) The number of patients was inadequate to assess the impact of stenting in the various morphologic subgroups. 7) Although repeat catheterization was requested by protocol of all patients 6 months after stent placement (or was performed earlier if an ischemic event occurred), only 42 of 59 surviving patients with stenting were eligible for late catheterization because of the relatively short duration of follow-up in this contemporary group, and only 79% of eligible patients consented to repeat catheterization. Late catheterization was not systematically performed in the control group; thus, overall angiographic follow-up was inadequate for restenosis rates to be adequately assessed or compared. However, evaluation of the actuarial incidence of clinical ischemic events was possible, as only two patients were lost to follow-up.

Conclusions. When compared with conventional therapy for abrupt closure, stenting produced a better angiographic

appearance at the site of occlusion and was more likely to restore normal distal coronary flow, thereby reducing the need for emergency bypass surgery. These data demonstrate, however, that immediate procedural benefit imparted by stenting may not necessarily translate into improvements in other in-hospital clinical end points such as death, myocardial infarction or intermediate-term freedom from cardiac events. Moreover, stenting in patients with threatened vessel closure may yield relatively minor benefit at the expense of a prolonged hospital stay and increased blood transfusion requirements. Prompt stent placement, rather than implantation only after failure of conventional treatment, may reduce the incidence and severity of postprocedure events after abrupt vessel closure. Randomized studies will be required to determine the relative efficacy of this management strategy.

References

1. de Feyter PJ, van den Brand M, Jaarman GJ, van Domburg R, Serruys PW, Suryapranata H. Acute coronary artery occlusion during and after percutaneous transluminal coronary angioplasty. Frequency, prediction, clinical course, management, and follow-up. Circulation 1991;83:927–36.
2. Lincoff AM, Popma JJ, Ellis SG, Hacker JA, Topol EJ. Abrupt vessel closure complicating coronary angioplasty: clinical, angiographic, and therapeutic profile. J Am Coll Cardiol 1992;19:926–35.
3. Black AJR, Nanney DL, Niederman AL, et al. Tear or dissection after coronary angioplasty. Morphologic correlates of an ischemic complication. Circulation 1989;79:1035–42.
4. Ellis SG, Roubin GS, King SB, et al. Angiographic and clinical predictors of acute closure after native vessel coronary angioplasty. Circulation 1988;77:372–9.
5. Bredlau CE, Roubin GS, Leimgruber PP, Douglas JS, King SB, Gruentzig AR. In-hospital morbidity and mortality in patients undergoing elective coronary angioplasty. Circulation 1985;72:1044–52.
6. Dotter CT. Transluminally-placed coilspring endarterial tube grafts: long-term patency in canine popliteal artery. Invest Radiol 1969;4:329–32.
7. Hearn JA, Douglas JS, Roubin GS, Ghazzal ZMB, Scott NA, King SB. Late outcome in patients receiving a balloon-expandable intracoronary stent for acute closure (abstr). Circulation 1991;84(suppl II):II-589.
8. Sigwart U, Urban P, Golf S, et al. Emergency stenting for acute occlusion after coronary balloon angioplasty. Circulation 1988;78:1121–7.
9. Haude M, Erbel R, Straub U, Dietz U, Schatz R, Meyer J. Results of intracoronary stents for management of coronary dissection after balloon angioplasty. Am J Cardiol 1991;67:691–6.
10. Roubin GS, Robinson KA. The Gianturco-Roubin stent. In: Topol EJ, ed. Textbook of Interventional Cardiology. Philadelphia: WB Saunders, 1990:633–46.
11. de Feyter P, DeScheerder I, van den Brand M, Laarman GJ, Suryapranata H, Serruys PW. Emergency stenting for refractory acute coronary artery occlusion during coronary angioplasty. Am J Cardiol 1990;66:1147–50.
12. Haude M, Erbel R, Straub U, Steffen W, Swars H, Meyer J. Subacute thrombotic occlusions after intracoronary implantation of Palmaz-Schatz stents: acute management and long-term outcome (abstr). Eur Heart J 1991;12:166.
13. Chesebro JH, Knatterud G, Roberts R, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Circulation 1987;76:142–54.
14. Califf RM, Phillips HR, Hindman MC, et al. Prognostic value of a coronary artery jeopardy score. J Am Coll Cardiol 1985;5:1055–63.
15. Ellis SG, Roubin GS, King SB, et al. In-hospital cardiac mortality after acute closure after coronary angioplasty: analysis of risk factors from 8,207 procedures. J Am Coll Cardiol 1988;11:211–6.
16. Holmes DR. Technical aspects. In: Vlietstra RE, Holmes DR, eds. Percutaneous Transluminal Coronary Angioplasty. Philadelphia: FA Davis, 1987:35–48.
17. Ellis SG, Vandormael MG, Cowley MJ, et al. Coronary morphologic and clinical determinants of procedural outcome with angioplasty for multivessel coronary disease: implications for patient selection. Circulation 1990;82:1193–202.
18. American College of Cardiology/American Heart Association Task Force. Guidelines for percutaneous transluminal coronary angioplasty. J Am Coll Cardiol 1988;12:529–45.
19. Detre KM, Holmes DR, Holubkov R, et al. Incidence and consequences of periprocedural occlusion. The 1985–1986 National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. Circulation 1990;82:739–50.
20. Sinclair IN, McCabe CH, Sipperly ME, Baim DS. Predictors, therapeutic options, and long-term outcome of abrupt reclosure. Am J Cardiol 1988;61:61G–6G.
21. Leitschuh ML, Mills RM, Jacobs AK, Ruocco NA Jr, LaRosa D, Faxon DP. Outcome after major dissection during coronary angioplasty using the perfusion balloon catheter. Am J Cardiol 1991;67:1056–60.
22. Pomerantz R, Kuntz R, Piana R, et al. Changing management of abrupt closure with perfusion balloon and laser balloon catheters (abstr). Circulation 1991;84(suppl II):II-131.
23. Stauffer JCh, Goy JJ, Kaufmann U, Kappenberger L. Treatment of post angioplasty occlusion with autoperfusion balloon catheter: an alternative to surgery (abstr)? Eur Heart J 1991;12:261.
24. Jenkins RD, Spears JR. Laser balloon angioplasty. A new approach to abrupt coronary occlusion and chronic restenosis. Circulation 1990;81(suppl IV):IV-101–8.
25. Mast EG, Bal ET, Ernst RM, Gin TJ, Ascoop CAPL, Plokker HWM. Laser balloon angioplasty for abrupt vessel closure during PTCA (abstr). Eur Heart J 1991;12:393.
26. Whitlow PL, Robertson GC, Rowe MH, et al. Directional coronary atherectomy for failed percutaneous transluminal coronary angioplasty (abstr). Circulation 1990;82(suppl III):III-1.
27. Zeiher AM, Kasper W, Gaissmaier C, Wollschlager H. Concomitant intracoronary treatment with urokinase during PTCA does not reduce acute complications during PTCA: a double-blind randomized study (abstr). Circulation 1990;82(suppl III):III-189.
28. Huber MS, Mooney JF, Madison J, Mooney MR. Use of morphologic classification to predict clinical outcome after dissection from coronary angioplasty. Am J Cardiol 1991;68:467–71.
29. Ellis SG, Myler RK, King SB, et al. Causes and correlates of cardiac death after unsupported coronary angioplasty—implications for the use of advanced support techniques. Am J Cardiol 1991;68:1447–51.
30. Talley JD, Weintraub WS, Roubin GS, et al. Failed elective percutaneous transluminal coronary angioplasty requiring coronary artery bypass surgery. In-hospital and late clinical outcome at 5 years. Circulation 1990;82:1203–13.
31. Buffet P, Danchin N, Villemot JP, et al. Early and long-term outcome after emergency coronary artery bypass surgery after failed coronary angioplasty. Circulation 1991;84(suppl III):III-254–9.
32. Ellis S, Debowey D, Bates ER, Topol EJ. Treatment of recurrent ischemia after thrombolysis and successful reperfusion for acute myocardial infarction: relation to in-hospital mortality and left ventricular function. J Am Coll Cardiol 1991;17:752–7.
33. Roubin GS, Cannon AD, Agrawal SK, et al. Intracoronary stenting for acute and threatened closure complicating percutaneous transluminal coronary angioplasty. Circulation 1992;85:916–27.
34. Ba'albaki HA, Weintraub WS, Tso V, et al. Restenosis after acute closure and successful reopening: implications for new devices (abstr). Circulation 1990;82(suppl III):III-134.
35. Tenaglia AN, Fortin DF, Frid DJ, et al. Restenosis and long-term outcome following successful treatment of abrupt closure during and after angioplasty (abstr). Circulation 1991;84(suppl II):II-130.
36. Heyndrickx GR, Amano J, Kenna T, et al. Creatine kinase release not associated with myocardial necrosis after short periods of coronary artery occlusion in conscious baboons. J Am Coll Cardiol 1985;6:1299–303.